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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/695,140	KUKOLJ ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *12-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040429*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

Applicant's claim in the Declaration of Inventorship and at the first page of the specification filed 28 October 2003 to priority under 35 U.S.C. § 119(e) of the 29 October 2002 filing date of US provisional application serial No. 60/421,943 is hereby acknowledged.

Information Disclosure Statement

Applicant's Information Disclosure Statement [IDS] filed with on 29 April 2004 is hereby acknowledged.

Restriction

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-11, drawn to at least one of several species of hepatitis C virus processing proteases comprising one or more amino acid substitutions that render the protease resistant to inhibition, classified in class 435, subclass 212.

II. Claims 12-15, drawn to polynucleotides encoding at least one of several species of hepatitis C virus processing proteases comprising one or more amino acid substitutions that render the protease resistant to inhibition, to vectors and host cells comprising same, and to a recombinant method of making the encoded protease utilizing such host cells, classified, *inter alia*, in class 526, subclass 23.2.

III. Claim 16, drawn to, a cellular method for determining the viability of an hepatitis C virus wherein the genome comprises a nucleic acid sequence encoding least one of several species of processing proteases comprising one or more amino acid substitutions that render the protease resistant to inhibition, classified in class 435, subclass 5.

IV. Claim 17, drawn to a cellular method for detecting an inhibitor compound capable of inhibiting a processing protease comprising one or more amino acid substitutions that render the protease resistant to inhibition activity utilizing a hepatitis C virus wherein the genome comprises a nucleic acid sequence encoding such a modified processing protease, classified in class 435, subclass 23.

V. Claim 18, drawn to an acellular method for detecting an inhibitor compound capable of inhibiting a processing protease comprising one or more amino acid substitutions that render the protease resistant to inhibition activity utilizing such a modified processing protease, classified in class 435, subclass 7.6.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group 1 and Group 2 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are independent chemical entities that are not disclosed as capable of use together, that have different modes of operation, different functions, and different effects, and that require separate searches in the patent and non-patent literature.

The invention of Group I is unrelated to the inventions of Groups III and IV. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventions of Groups III and IV require the presence of a hepatitis C virus genome to infect a cell to conduct a method and may not utilize a modified protease alone, thus the different inventions are not disclosed as capable of use together also have different modes of operation.

Inventions of Groups I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product, such as the *in vitro* processing of unlabelled peptide and polypeptide substrates.

Inventions of Groups II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product, such as a cellular method for detecting an inhibitor compound capable of inhibiting a processing protease.

Inventions of Groups II and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1)

the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product, such as cellular method for determining the viability of an hepatitis C virus wherein the genome comprises a nucleic acid sequence encoding a modified processing protease.

Inventions of Groups II and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together and also have different modes of operation.

Inventions of Groups III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation where they are independent methods having different steps using different reagents.

Inventions of Groups III and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation where they are independent methods having different steps using different reagents.

Inventions of Groups IV and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of use together have different modes of operation where they are independent methods having different steps using different reagents.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention:

Groups I and V comprise products and methods of use requiring any of several disclosed species of modified processing proteases where a first species comprises an amino acid substitution in a hepatitis C virus processing protease in least one position selected from the positions 155, 156, and 168 numbered according to the amino acid sequence set forth in SEQ ID NO:2 and further, optionally, comprises an amino acid substitution selected from the group of: no further substitution, S20N, R26K, Q28R, A39T, Q41R, I71V, Q80R, Q86R, P89L, P89S, S101N, A111S, P115S, L144F, A150V, V158L, E176K, T178S, M179I, M179V, M179T, and S122R, where the positions for substitutions are numbered according to the amino acid sequence set forth in SEQ ID NO:2.

Thus an election of either Group I or Group V must indicate a species of modified protease with a first substitution at one of the positions 155, 156, and 168, and also indicate second substitution selected from the group of: no further substitution, S20N, R26K, Q28R, A39T, Q41R, I71V, Q80R, Q86R, P89L, P89S, S101N, A111S, P115S, L144F, A150V, V158L, E176K, T178S, M179I, M179V, M179T, and S122R.

Groups II, III, and IV comprises products and methods of use requiring any of several disclosed species of polynucleotides encoding modified processing proteases where a first species comprises an amino acid substitution in a hepatitis C virus processing protease in least one position selected from the positions 155, 156, and 168 numbered according to the amino acid sequence set forth in SEQ ID NO:2 and further, optionally, comprises an amino acid substitution selected from the group of: no further substitution, S20N, R26K, Q28R, A39T, Q41R, I71V, Q80R, Q86R, P89L, P89S, S101N, A111S, P115S, L144F, A150V, V158L, E176K, T178S, M179I, M179V, M179T, and S122R, where the positions for substitutions are numbered according to the amino acid sequence set forth in SEQ ID NO:2.

Thus an election of one of Groups II, III or IV must indicate a polynucleotide that encodes a of modified protease with a first substitution at one of the positions 155, 156, and 168, and also indicate second substitution selected from the group of: no further substitution, S20N, R26K, Q28R, A39T, Q41R, I71V, Q80R, Q86R, P89L, P89S, S101N, A111S, P115S, L144F, A150V, V158L, E176K, T178S, M179I, M179V, M179T, and S122R.

Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is

finally held to be allowable. Currently, claims 1-17 are generic because no claim requires a single substitution at just one of the positions 155, 156, and 168, whether or not it is combined with another substitution at another position recited in claim 8.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103(a) of the other invention.

Election

During a telephone conversation with Mr. David A. Dow on 8 September 2005 a provisional election was made **with** traverse to prosecute the invention of Group I, claims 1-11 wherein a further election was made of a species of HCV protease having a first amino acid substitution at a position 156 and wherein at least a second substitution is the P89S substitution. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention and claims 1-11 are examined herein to the extent they read on the provisionally elected species of substituted proteases.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one

or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Notice of Requirements for Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.** Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. §§101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. §121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Objections

Compliance with 37 CFR § 1.821 is required in response to this Office action. Claims 1-5 are objected to because they lack a designation of a particular sequence according to the requirements of 37 CFR § 1.821 for a Sequence Disclosure wherein the enumerated positions can be identified. Even if a sequence were set forth in the

claims - so that one could recognize where to start counting to arrive at the recited positions - recitations involving a nucleotide or amino acid sequence positions must also include a statement of the designation, "**SEQ ID NO:n**", where "n" is an integer corresponding to the Sequence Disclosure. See 37 CFR §§ 1.821(b), (c) and (d).

Claims 1-5 and 9 are objected to because of the following informalities: Claims 1 and 2 repeat the preposition "at", see the first line of claim 1 and the second line of claim 2, and claim 1 further lacks the proper use of the indefinite article "an" before the term, "amino acid", at line 1 of the claim. Appropriate correction is required, e.g., "[a] modified HCV NS3 domain protease amino acid sequence wherein the modification comprises at least one amino acid substitution at one or more positions selected from the group consisting of positions that correspond to positions 155, 156, and 168 of SEQ ID NO:2." It is noted that adopting this recitation will require changing each occurrence of "mutation" in the dependent claims to "modification" but need not require changing the term "replaced" to "substituted" as the terms are synonymous.

Claims 3-5 and 9 lack the proper use of the indefinite article "the" before the term, "amino acid", at lines 1 of each claim. Appropriate correction is required, e.g., amending each claim to recite "the amino acid".

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-9 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-9 do not describe a "new . . . composition of matter" as the statute requires because they fail to distinguish NS3 proteases present in Nature and mutated by natural processes from NS3 proteases that are discoveries, an invention reduced to practice by the efforts of a person. This rejection may be overcome by amending claims 1, 6 and 9

to add an appropriate distinguishing term to state statutory subject matter, e.g., reciting either "[a]n **isolated** NS3 protease" or, as indicated in the objection above to claims 1 and 2, "[a] **modified** HCV NS3 domain protease". This latter amendment is improved by replacing each occurrence of "mutation" in the elected claims with "substitution".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to exemplify or describe the preparation of the divergent proteases of claims 1-5 where these claims reach generic proteases that may differ at any or all of the amino acid positions of a protease that, prior to a recited modification, has no particular structure and no particular, defined, function. Claims 9-11 are not subject to this rejection because they recite a structural limitation, "90% identity", that accurately reflects a portion of the naturally-occurring sequence diversity in NS3 domain regions of polyproteins encoded by naturally-occurring HCV isolates in the prior art, such as the HCV strains JT, J, Taiwan, JK1, HCV-1, and H. Indeed, the arginine at the position corresponding to position 155 and the alanine at the position corresponding to position 156 are both strictly conserved, and the aspartate at the position corresponding to a position 168 of SEQ ID NO:2 is highly conserved, thus each is readily identified in NS3 domain regions of polyproteins encoded by prior art HCV isolates even though a corresponding NS3 domain shares only 76% identity with SEQ ID NO:2 herein. See Results Nos. 1-11 in the PIR 79 database sequence search results scanned into the

record with the search history accompanying this communication. See also Figure 4 of Yamada et al., made of record herewith.

Because claims 1-5 state neither a structural requirement nor any particular functional requirement, they are construed to reach "mutations" present in one, two, or three positions identifiable to no particular protease. Neither the claims or the specification, nor the prior art of record, describe or suggest the structure of a generic, unidentified, protease amino acid sequence before a "mutation" nor what the differences might be between such a generic protease and a disclosed protease amino acid sequence and the specification does not otherwise disclose or suggest the nature of any of the generic proteases that meet limitations of the claims. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of proteases of claims 1-5 diverging anywhere, in any fashion from the sequence of SEQ ID NO:2 wherein any of the 18 recited positions intended for modification can be identified for a "mutation".

Claims 1-5 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for modification of HCV NS3 domain protease amino acid sequence by one or more amino acid substitutions at positions corresponding to positions 155, 156 and 168 of SEQ ID NO:2 to produce a proteolytically active NS3 domain protease, wherein the HCV NS3 domain prior to modification is capable of associating with an HCV NS4A domain cofactor in a complex mediating the cleavage of the HCV NS4B, NS5A and NSSB domains from a HCV polyprotein, does not reasonably provide enablement for modifying a generic protease by making amino acid substitutions at positions corresponding to positions 155, 156 and 168 of SEQ ID NO:2 to produce a proteolytically active NS3 domain protease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In view of the recitation of the term "mutation" in claim 1, claims 1 and 2 must be construed to reach amino acid additions and deletions as well as the disclosed amino

acid substitutions separately recited in, e.g., claims 3-5. In addition, for the reasons explained above claims 1-5 contemplate modifications in generic proteases that need have no particular structure prior to modification nor have a particular proteolytic activity prior to modification. The specification does not support the introduction of amino acid additions or deletions at one or more positions corresponding to positions 155, 156 and 168 of SEQ ID NO:2 and the strict conservation of the arginine and alanine at positions 155 and 156, and the functional conservation of aspartate, glutamate or the hydrophilic glutamine at position 168, in all native HCV NS3 proteases in the prior art clearly indicates that additions or deletions of these amino acids at these positions may compromise the proteolytic activity of the polypeptide. See page 13, lines 19-26, of the specification. Further, in reciting "protease", the claims require an active protease, and the specification also discloses that the nature of the intended invention is modification of a HCV NS3 protease to make it more resistant to protease inhibition than a native HCV NS3 protease. See Koch et al., 1997, made of record with Applicant's Information Disclosure Statement, who disclose that an R155S substitution provides an active HCV NS3 domain protease having no alteration of substrate specificity. See also, Lahm et al., 2002, made of record with Applicant's Information Disclosure Statement, who discuss the contribution of R155 for active site conformation at page 288.

The specification fails to teach that amino acid additions or deletions at positions in a native HCV NS3 domain protease that correspond to positions 155, 156, and 168 of SEQ ID NO:2 can provide a functioning protease and the specification does not teach how to identify the recited positions for disclosed amino acid substitutions where they are made in a generic protease that need have no defined structural relationship to SEQ ID NO:2 and has no requirement for any specific proteolytic activity. Mere sequence perturbation cannot enable design and preparation of a myriad of divergent proteases

yet provide the public with a protease that retains the catalytic activity of a native HCV NS3 protease.

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (discussing eight factors relevant to analysis of enablement). Applying the factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering generic protease amino acid sequences either structurally unrelated to SEQ ID NO:2 or functionally unrelated to SEQ ID NO:2 to the extent recited in the claims,

b) the specification lacks guidance for altering protease amino acid sequences structurally related to SEQ ID NO:2 by amino acid deletions or additions at one or more of the positions recited in claim 1 in order to provide a functioning protease,

b) the specification lacks working examples wherein generic proteases either structurally unrelated to SEQ ID NO:2 or functionally unrelated to SEQ ID NO:2, are altered at positions recited in claim 1, and lacks working examples wherein generic proteases structurally related to SEQ ID NO:2 are altered by amino acid deletions or additions at positions recited in the claim 1, to provide a functioning protease,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no HCV NS3 domain proteases have been altered by amino acid deletions or additions at positions recited in the claim 1, or where generic proteases have had any of the amino acid positions recited in claim 1 identified as corresponding to positions ins SEQ ID NO:2.

Thus the scope of subject matters embraced by the phrase, "of the native HCV NS3 protease is mutated", is unsupported by the present specification even if taken in combination with teachings available in the prior art.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 are indefinite because claim 1 recites "comprised of an amino acid sequence in which . . . the native HCV NS3 protease is mutated" because, without anyd reference to an original, or initial, amino acid sequence, the artisan and public seeking to determine the metes and bounds of the intended subject matter cannot tell whether a change produces a claimed amino acid sequence where the amino acid sequence of a "native HCV NS3 protease" is itself a "variant" or "mutant" by comparison with another "native HCV NS3 protease". See Results Nos. 1-11 in the PIR 79 sequence search results made of record with the search history accompanying this communication.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1 and 5 are rejected under 35 U.S.C. § 102(a) as being anticipated by Migliaccio et al., 2002, cited in Applicant's priority application serial No. 60/421,943, who disclose that the amino acid substitutions D168A, D168Y, and D168V, where position 168 corresponds to position 168 in SEQ ID NO:2 herein, provide an active HCV NS3 domain protease, meeting limitations of claims 1 and 5. See Abstract.

Claims 1-3 are rejected under 35 U.S.C. § 102(b) as being anticipated by Koch et al., 1997, made of record with Applicant's Information Disclosure Statement, who

disclose that the amino acid substitution R155S, where position 155 corresponds to position 155 in SEQ ID NO:2 herein, provides an active HCV NS3 domain protease having no alteration of substrate specificity, meeting the limitations of claims 1-3. See Figure 1A at page 80.

Claim 1 is rejected under 35 U.S.C. § 102(b) as being anticipated by Beyer et al., published online on 9 February 2001 and made of record herewith, who disclose that the amino acid substitutions D168Q and D168E, where position 168 corresponds to position 168 in SEQ ID NO:2 herein, provides an active HCV NS3 domain protease, meeting the limitations of claim 1. See the discussion at pages 86 and 87.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
27 March 2005

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER